

**Vitamin D
25-Hydroxycalciferol
(Vitamin D2 and
Vitamin D3)**

A Test for Assessing Vitamin D Sufficiency

- Vitamin D deficiency is associated with a variety of disease states.
- Vitamin D deficiency is common in the normal population.
- Vitamin D deficiency is commonly found in patients suffering from End-Stage Renal Disease (ESRD).
- Vitamin D deficiency responds to treatment in renal patients.

Vitamin D Metabolism

Although vitamin D can be obtained from the sun, food or vitamin supplements, vitamin D deficiency remains common in the general population.¹ Vitamin D occurs in two forms, vitamin D2 and vitamin D3. Vitamin D2 (ergocalciferol) is derived from plants and vitamin D3 (cholecalciferol) is the natural animal form.² Both forms are available as vitamin supplements. Whatever the source, vitamin D is hydroxylated in the liver to 25-hydroxy-vitamin D, which is the main circulating form of vitamin D and is the best indicator of vitamin D nutritional status.^{1, 28, 29} It is the form of vitamin D that is measured in the laboratory.

25-hydroxy-vitamin D is acted upon by an enzyme, primarily in the kidney, but also in many other tissues, converting it to its physiologically active form, 1,25-dihydroxy-vitamin D.¹ This physiologically active vitamin mediates the absorption of calcium in the kidney and intestines.² Vitamin D increases intestinal transport of calcium and phosphate, and suppresses PTH secretion.²⁹ Hypercalcemia can oversuppress PTH, leading to adynamic bone disease absorption (ABD), increasing the risk of fracture.²⁹ An increase in phosphorus due to increased absorption caused by vitamin D, is usually treated with phosphate binders or prolonged dialysis sessions. Dialysis patients with preexisting ABD are at risk of vascular calcification if high doses of vitamin D are administered. Lower doses may have a protective effect.⁴

Vitamin D Related Diseases in the General Population

Bone diseases directly associated with vitamin D deficiency include rickets⁵, osteomalacia⁶ and osteoporosis.⁷ Low levels of vitamin D can be associated with coronary artery disease^{8,9}, muscle weakness^{10, 11, 12}, breast cancer¹³, colorectal cancer^{14, 15} and diabetes.^{16, 17, 18} Vitamin D functions through a vitamin D receptor (VDR) present in the tissues associated with mineral metabolism, and also in colon, skin, lymph node, pituitary gland, ovary and the immune system. Approximately 3% of the human genome is either regulated directly or indirectly by the vitamin D system.³ This may explain why vitamin D appears to play a role in many diseases.⁴

Low patient levels of vitamin D are associated with increased mortality^{19, 20}, and moderate doses (400-800 IU/day) of vitamin D resulted in a 7% reduction in total mortality in one study.²⁸

Clinical Applications of Vitamin D Testing

Evaluate the vitamin D status of the patient. Most authors recommend a 25-hydroxy-vitamin D level above 30 IU as optimum.

Vitamin D deficiency is common in dialysis patients and is correctable.

Relevance in Patients with Kidney Disease

Investigations into the value of vitamin D in dialysis patients are in the early stages. Typically, CKD and ESRD patients have low levels of vitamin D.^{20-24, 26} The condition is correctable with the administration of vitamin D supplements.^{25, 26} In one study, correcting the deficiency decreased bone turnover, increased albumin levels, and brought more patients within the KDOQI guidelines for calcium and phosphorus. In another three year prospective study of peritoneal dialysis patients, those with the lowest serum levels of vitamin D had an increased risk of cardiovascular events.²⁷

Supplemental vitamin D has a wide therapeutic window in the general population. However, in renal patients, the active hormone form of vitamin D, calcitriol, and the vitamin D analogs that bind directly to the vitamin D receptor are highly potent and have a narrow therapeutic window.²⁹ Secondary hyperparathyroidism is one result of the inability to activate 25-hydroxy-vitamin D after renal function is lost.²⁹

In most cases, moderate supplemental vitamin D therapy provides a protective role in cardiovascular disease, independent of its effects on mineral metabolism, and results in improved longevity in both the general and the dialysis population.²⁹ Nonetheless, because vitamin D increases intestinal absorption of calcium and phosphorus and suppresses PTH, high doses of vitamin D are contraindicated in the following conditions.²⁹

- Hypercalcemia
- Hyperphosphatemia
- Low PTH levels
- Adynamic bone disease (ABD)
- Preexisting vascular calcification

The overall benefit of maintaining an adequate vitamin D level in dialysis patients should be weighed against the potential risk of development of vascular calcification or adynamic bone disease. However, there is general agreement that low doses of oral vitamin D supplements (400-800 IU/day) provide the greatest benefit to dialysis patients and avoid the potential toxicity associated with the administration of higher doses of vitamin D.

Test Methodology

Vitamin D is measured by chemiluminescence assay, which detects 100% of both vitamin D2 and vitamin D3.

Interpretation of Results

The definition of vitamin D status has been recently updated.

Deficiency	<10 ng/mL	(0-25 nmol/L)
Insufficiency	10-30 ng/mL	(25-75 nmol/L)
Sufficiency	30-100 ng/mL	(75-250 nmol/L)
Toxicity	>100 ng/mL	(>250 nmol/L)

Specimen Collection

Specimen Requirement:	0.5 mL serum (SST GEL tube)
Other Requirements:	Fasting specimens are recommended, but not required.
Methodology:	Chemiluminescence
Interferences:	Hemolysis and Lipemia
TAT:	1 Day
Test Set-up:	M-Sat
CPT Code:	82306



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